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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/993,333 | 11/14/2001 | Larry Wayne Oberley | 875.042US1 | 5690 |

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SCHWEGMAN, LUNDBERG, WOESSNER & KLUTH, P.A.
P.O. BOX 2938
MINNEAPOLIS, MN 55402

| EXAMINER | |
|---|---|
| SCHULTZ, JAMES | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | |

DATE MAILED: 04/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

F-6

| Office Action Summary | Application No. 09/993,333 | Applicant(s) OBERLEY ET AL. | |
|---|---|---|---|
| | Examiner J. Douglas Schultz | Art Unit 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *06 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,5-8 and 11-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-8 and 11-19* is/are rejected.

7)☒ Claim(s) *20 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 October 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Response to Arguments*

Applicant's response filed February 6, 2003 has been considered. Rejections and/or objections not reiterated from the previous office action mailed June 18, 2002 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Applicant's election with traverse of SEQ ID NO: 2 in new claim 20, made in Paper No. 13 filed February 6, 2003 is acknowledged. The traversal is on the ground(s) that because the 3 new sequences submitted by applicants overlap, that a serious search burden is therefore not imposed on the Office. Furthermore, because current Office policy allows up to 10 independent and distinct nucleotides to be examined in a single application, applicant contends that a search for all three nucleotides sequences does not impose a burden. This is not found persuasive because as stated previously, to search more than one nucleotide sequence does impose a burden, because each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of the antioxidant enzyme start codon, and each antisense, upon binding to the antioxidant enzyme start codon, functionally modulates (increases or decreases) the expression of the gene and to varying degree. Each sequence requires that independent analyses and searches be performed, with potentially unique prior art references that may apply. Finally, applicant states that since claim 20 recites the three sequences under consideration in Markush format, that they therefore constitute different species; as pointed out in the previous Office action, each sequence is considered independent and distinct, and each therefore constitutes different inventions, not species, and is considered accordingly.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-19 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the same reasons of record as set forth in the Office action dated June 18, 2002.

Applicant has traversed the rejection of claims 1-19. Said claims had been rejected for lacking adequate written description for the broad genus of antioxidant enzymes encompassed in the claims, specifically any allele, mutant, or homolog of any catalase, copper and zinc superoxide dismutase, manganese superoxide dismutase, phospholipid or cytosolic glutathione peroxidase from any species. Applicant argues that the specification lists the name of said enzymes, and also provides 7 specific constructs that bind to three of the enzymes, which applicant claims provides adequate written description.

These arguments are not considered persuasive. At the outset, it is noted that applicant believes that the examiner mistakenly assumed that applicant was claiming said genus of antioxidant enzymes. Applicant is directed to the last paragraph on page 5 of the Office action dated June 18, 2002, wherein it is stated that in order to make applicants' claimed antisense sequences, one must first have adequate description of the targets in order to formulate such antisense sequences. It is clear that applicant is not claiming the instantly contemplated

antioxidant enzymes; it is also clear that one must have knowledge of their sequence, however, to make and use the antisense oligos as instantly claimed.

Regarding applicants arguments that a listing of names of antioxidant enzymes constitutes adequate disclosure, it is reiterated that applicants broad language encompasses targeting any start codon of any catalase, copper and zinc superoxide dismutase, manganese superoxide dismutase, phospholipid or cytosolic glutathione peroxidase of any allele, mutant and homolog from any species; clearly, reciting the name of an antioxidant enzyme does not provide one of skill in the art with the structural information necessary to make and use antisense to such a broad genus. Applicants assertion that the disclosure of 7 antisense oligos targeting three of the five named targets constitutes adequate written description for the claimed invention is not adopted, because for reasons given above, and given that each of the five target enzymes is structurally independent from each other, the genus is expected to be exceedingly large and diverse. A representative sample of antisense to such a broad genus must reflect this breadth and diversity, which applicants' constructs do not.

Claims 8, and 11-19 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vivo* antisense-mediated inhibition of human superoxide dismutase in the treatment of tumors, does not reasonably provide enablement for said inhibition of any/all antioxidant enzymes, or to treat heart disease, arthritis, or neurodegenerative diseases, for the same reasons of record as set forth in the Office action mailed June 18, 2002. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants have amended claim 8 to incorporate claim 10, which had subject matter that was indicated as enabled. However, applicants have not amended claim 8 to address the breadth of the antioxidants claimed, which comprised a fundamental basis of the previous rejection. Accordingly, and since no other arguments have been presented, the claims above stand rejected as lacking enablement for reasons of record.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 7, 18, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 7, 18, and 19 depend on independent claims 1 or 8. Said independent claims are drawn to an oligonucleotide 18 to 26 nucleotides long or method of using thereof. Claims 6, 7, 18, and 19 claim an oligo that is complementary to either 90% or 100% of its target. Since independent claims 1 and 8 stipulate that the claimed oligos must be between 18 and 26, and since the target of claims 6, 7, 18, and 19 is much larger than 26 nucleotides, any oligo that is

complementary to 90% or 100% to said target will also be much longer than 26 nucleotides, rendering the length of the oligos of claims 6, 7, 18, and 19 indefinite.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Sugino et al. (Biology of Reprod. 1999. Vol. 61:1133-1138).

The invention of the above claims is drawn to an antisense oligonucleotide 18-26 nucleotides long that targets the start codon of catalase, copper and zinc superoxide dismutase, manganese superoxide dismutase, phospholipid or cytosolic glutathione peroxidase, or wherein said oligo is about 20 nucleotides long.

Sugino et al. teaches an antisense oligonucleotide 21 nucleotides long that targets the start codon of copper and zinc superoxide dismutase, and thus anticipates the instant claims.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 3, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over either of Ferguson-Kohout et al. (FASEB J. 1996. 10(3)3067) or Bauman et al. (Teratology 1996. 53(2)84), in view of Baracchini et al. (U.S. Patent Number 5,801,154).

The invention of the above claims is drawn to an antisense oligonucleotide 18-26 nucleotides long that targets the start codon of catalase, copper and zinc superoxide dismutase, manganese superoxide dismutase, phospholipid or cytosolic glutathione peroxidase, or wherein said oligo is about 20 nucleotides long, or is phosphorothiolated.

Ferguson-Kohout et al. and Bauman et al. teach antisense inhibition of catalase and glutathione peroxidase, respectively. Ferguson-Kohout et al. and Bauman et al. do not teach said inhibition comprising phosphorothiolated oligonucleotides 18-26 nucleotides long that target the start codon.

Baracchini et al. teach antisense inhibition of mRNA transcripts using phosphorothiolated oligonucleotides that target the start codon, and are between 8 and 30 nucleotides long.

It would have been obvious to one of ordinary skill in the art to modify the antisense of either Ferguson-Kohout et al. or Bauman et al. in the manner of Baracchini et al. One of ordinary skill in the art would have been motivated to do so because Baracchini et al. expressly teach the applicants' instantly claimed oligo length, and also teach that the start codon is a preferred targeting site. Furthermore, Baracchini et al. teach that incorporating phosphorothioate modifications confers resistance to degradation and enhances the bioactive half-life. One would have had a reasonable expectation of success, because Baracchini et al. teach the steps involved in such targeting and modifications, and since these modifications are routine to one of ordinary skill in the art. Therefore, in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

***Allowable Subject Matter***

Claims 20 and 21 are objected to as containing withdrawn subject matter (i.e. SEQ ID NOS: 1 and 3), but would be allowable if SEQ ID NO: 2 were rewritten in a claim in independent form including all of present limitations, because a sequence search has revealed no prior art against SEQ ID NO: 2.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Douglas Schultz whose telephone number is 703-308-9355. The examiner can normally be reached on 8:00-4:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on 703-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

James Douglas Schultz, PhD
April 17, 2003

ANDREW WANG
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600